ECP 2018

No conflict of interest

Impact of Race/Ethnicity on Oncogenic Driver Mutations Prevalence and Outcomes in Thyroid Nodules

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Background:

- Thyroid cancer has become the most common endocrine malignancy, with an increasing incidence over the past 20 years.
- In the United States, thyroid cancer is expected to account for 3.8% of new cancer diagnoses.
- Many factors can impact clinical behavior of thyroid carcinoma subtypes including **sex, age, oncogenic drivers, and race/ethnicity**
- A previous study showed evidence of racial disparities in clinical behavior of thyroid carcinoma subtypes

Tang et al. World Journal of Surgical Oncology (2018) 16:45
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World Journal of Surgical Oncology

RESEARCH Open Access

Racial disparities of differentiated thyroid carcinoma: clinical behavior, treatments, and long-term outcomes

Jianing Tang[1], Deguang Kong[2], Qiuxia Cui[1], Kun Wang[3], Dan Zhang[3], Xing Liao[1], Yan Gong[4*] and Gaosong Wu[1*]

Result: Black Americans had a worse overall survival than white Americans (HR = 1.127, $P = 0.002$). While disease-specific survival (DSS) was comparable, the risk factors for DSS were different between white and black Americans. Black Americans had less lymph node metastasis of classical variant papillary thyroid carcinoma (CPTC, OR = 0.476, $P < 0.001$) and follicular variant papillary thyroid carcinoma (FVPTC, OR = 0.522, $P < 0.001$), but not follicular thyroid carcinoma (FTC). However, black Americans with FVPTC, but not CPTC or FTC, had a higher potential of distant metastasis (OR = 1.715, $P = 0.026$). Furthermore, only white patients with tumor > 2 cm and lymph node metastasis benefited from radioactive iodine.

Conclusions: The risk factors for DSS were significantly different in white and black patients. The impact of race should be considered in treatment strategy for thyroid cancer.

Background:

- The discovery of oncogenic drivers and mutations started a new era for thyroid cancer management . But the role of these mutations in different racial/ethnic populations has been understudied.

Objectives:

We aimed to evaluate the racial disparities impact on oncogenic driver mutations in a subset of thyroid neoplastic lesions.

Specifically:

To evaluate the prevalence of the common mutations/gene fusion alterations in a subset of thyroid neoplastic lesions for race/ethnicity subgroups

Also, I will share the results showing the impact of racial/ ethnic disparity of pre-operative risk classification predictability using ThyroSeq V2 NGS testing. (USCAP 2018 Abstract)

Study: Thyroid nodules

- 1157 thyroid nodules with corresponding fine needle aspiration biopsy (FNAs) performed at Boston medical center between February 2015 and September 2017.
- 482 Thyroid nodules with corresponding ThyroSeq next generation performed .
- 58 fine needle aspiration biopsies were excluded because the diagnostic material for molecular analysis was insufficient or had an indeterminate result.
- The total were included in this analysis was **424 thyroid nodules**

Demographics:

- **Sex:**
  - Male = 73 (17%)
  - Female= 351 (83%)
- **Age=** rang (12-94 years old)

- **Race and ethnicity ;** Patients were grouped into 5 cohorts:
  - Non- Hispanic/Latino White = 123 (29%)
  - Non- Hispanic/Latino Black = 131 (31%)
  - Hispanic/Latino = 83 (20%)
  - Asian = 28 (10%)
  - Other= 59 (12%)

- If patients self-identified as both Hispanic/Latino and another race, they were included in the study as Hispanic/Latino.

ThyroSeq test results:

- Specific name of Mutation /gen fusion
- Negative
- Currently negative

Negative test

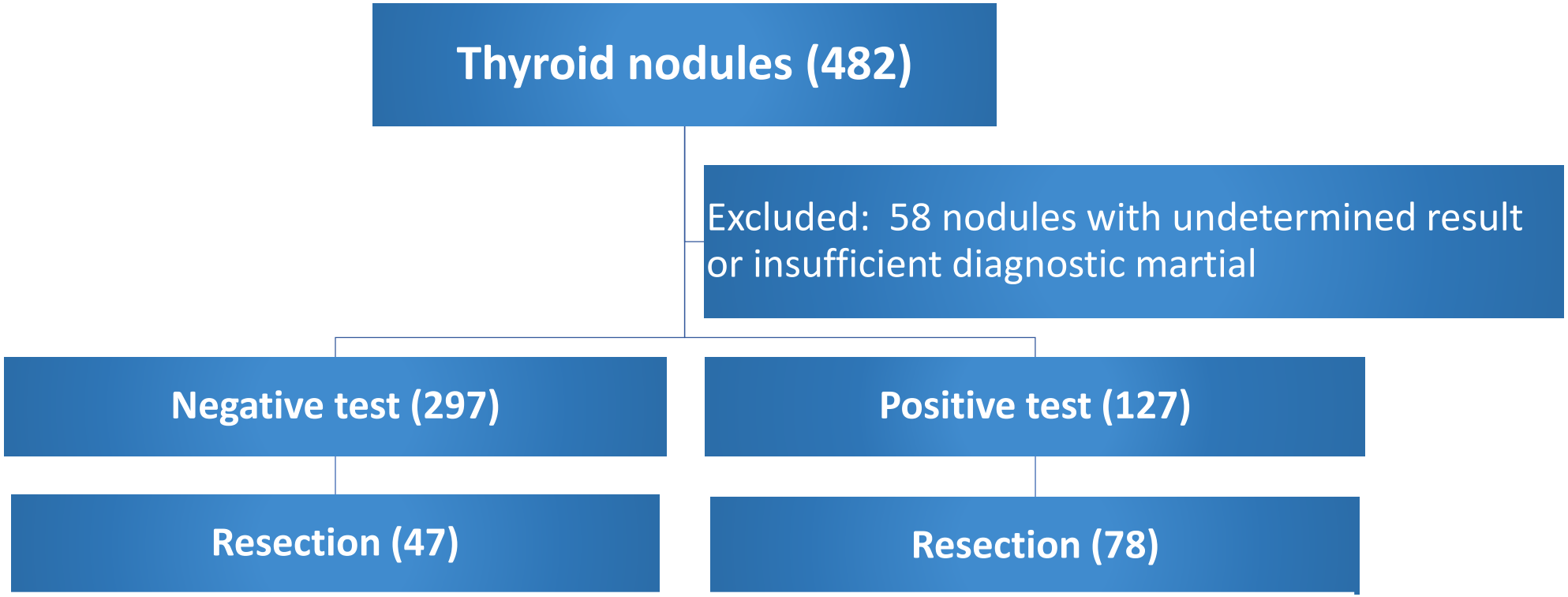
- Isolated RAS or RAS-like mutation
- Isolated BRAF V600E or BRAF V600E-like mutation
- Multiple high-risk (HR) mutations

Positive Test

Variables	Non-Hispanic White (n= 123)	Non-Hispanic Black (n= 131)	Hispanic/Latino (n=83)	Asian (n= 28)	Others (n=59)	P*
Age, median (range)	55 (22-87)	53 (23-94)	47 (19-82)	50 (26-70)	50 (12-87)	0.021
Sex						
Female	94 (76%)	119(91%)	69(83%)	26(93%)	43(73%)	0.004
Male	29(24%)	12(9%)	14(17%)	2(7%)	16(27%)	

	Race/ethnicity					
Variables	Non-Hispanic White (n= 123)	Non-Hispanic Black (n= 131)	Hispanic/Latino (n=83)	Asian (n= 28)	Others (n=59)	P*
Bethesda-I	14 (11%)	16(12%)	8(10%)	6(21%)	8(14%)	0.185
Bethesda-II	20(16%)	41(31%)	17(20%)	3(11%)	12(20%)	
Bethesda-III	71(58%)	65(50%)	45(54%)	17(61%)	35(59%)	
Bethesda-IV	10(8%)	5(4%)	6(7%)	0(0%)	1(2%)	
Bethesda-V	5(4%)	1(1%)	3(4%)	2(7%)	2(4%)	
Bethesda-VI	3(3%)	3(2%)	4(5 %)	0(0%)	1(2%)	

	Race/ethnicity					
ThyroSeq test	Non-Hispanic White (n= 123)	Non-Hispanic Black (n= 131)	Hispanic/Latino (n=83)	Asian (n= 28)	Others (n=59)	P*
Positive	45(37%)	30 (23%)	24(29%)	12(43%)	16(27%)	0.084
Negative	78(63%)	101(77%)	59(71%)	16(57%)	43(73%)	
Surgical Resection						
No	82(67%)	97(74%)	53(64%)	20(71%)	47(80%)	0.21
Yes	41(33%)	34(26%)	30(36%)	8(29%)	12(20%)	


Thyroid nodules (482)
Excluded: 58 nodules with undetermined result or insufficient diagnostic martial
Negative test (297)
Positive test (127)
Resection (47)
Resection (78)

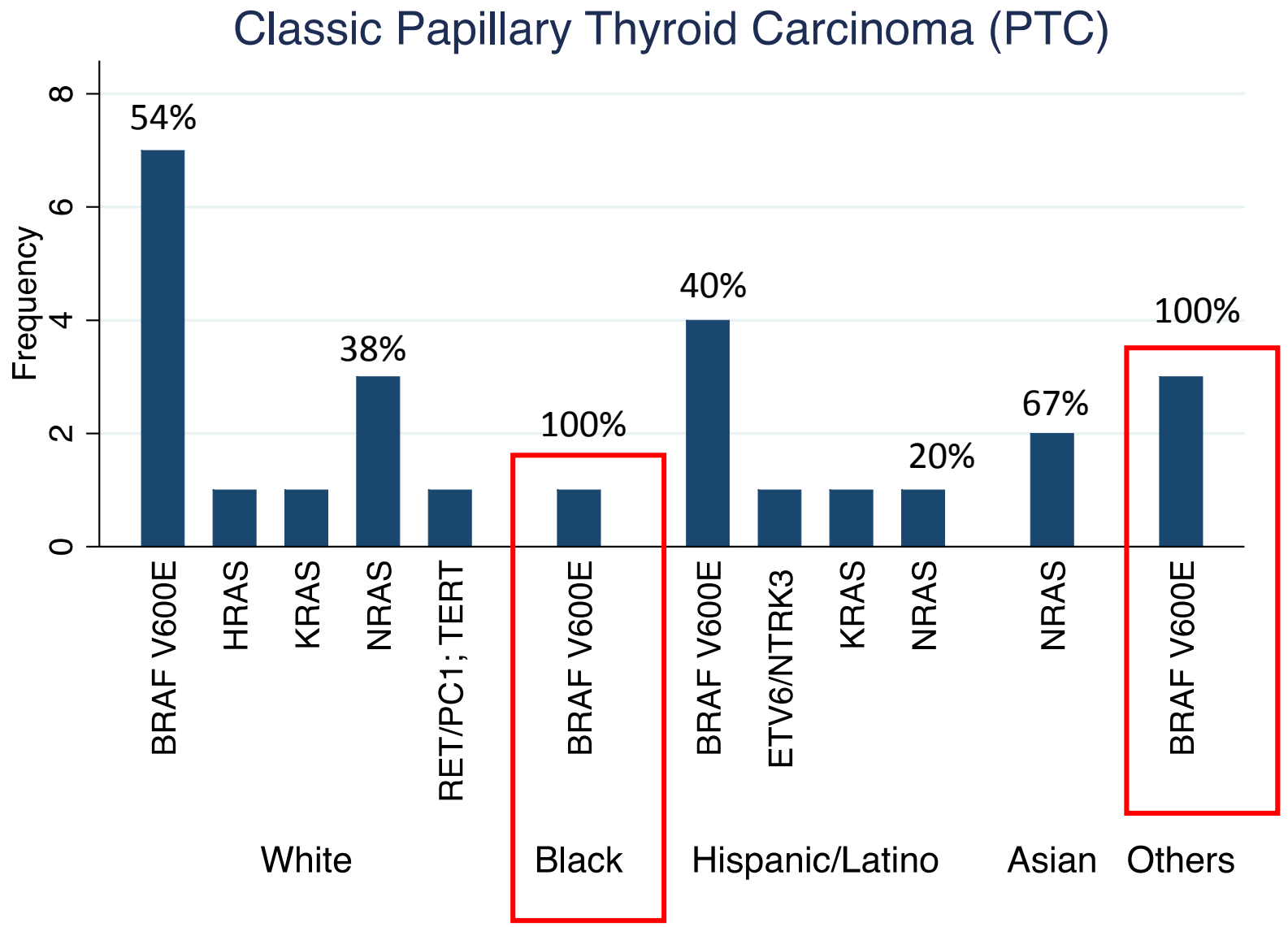
Histological Diagnosis :

- Papillary thyroid cancer - classic variant
- Papillary thyroid cancer – Follicular varian
- Poorly differentiated carcinoma
- Follicular carcinoma
- Medullary thyroid cancer
- Adenomas
- NIFTP

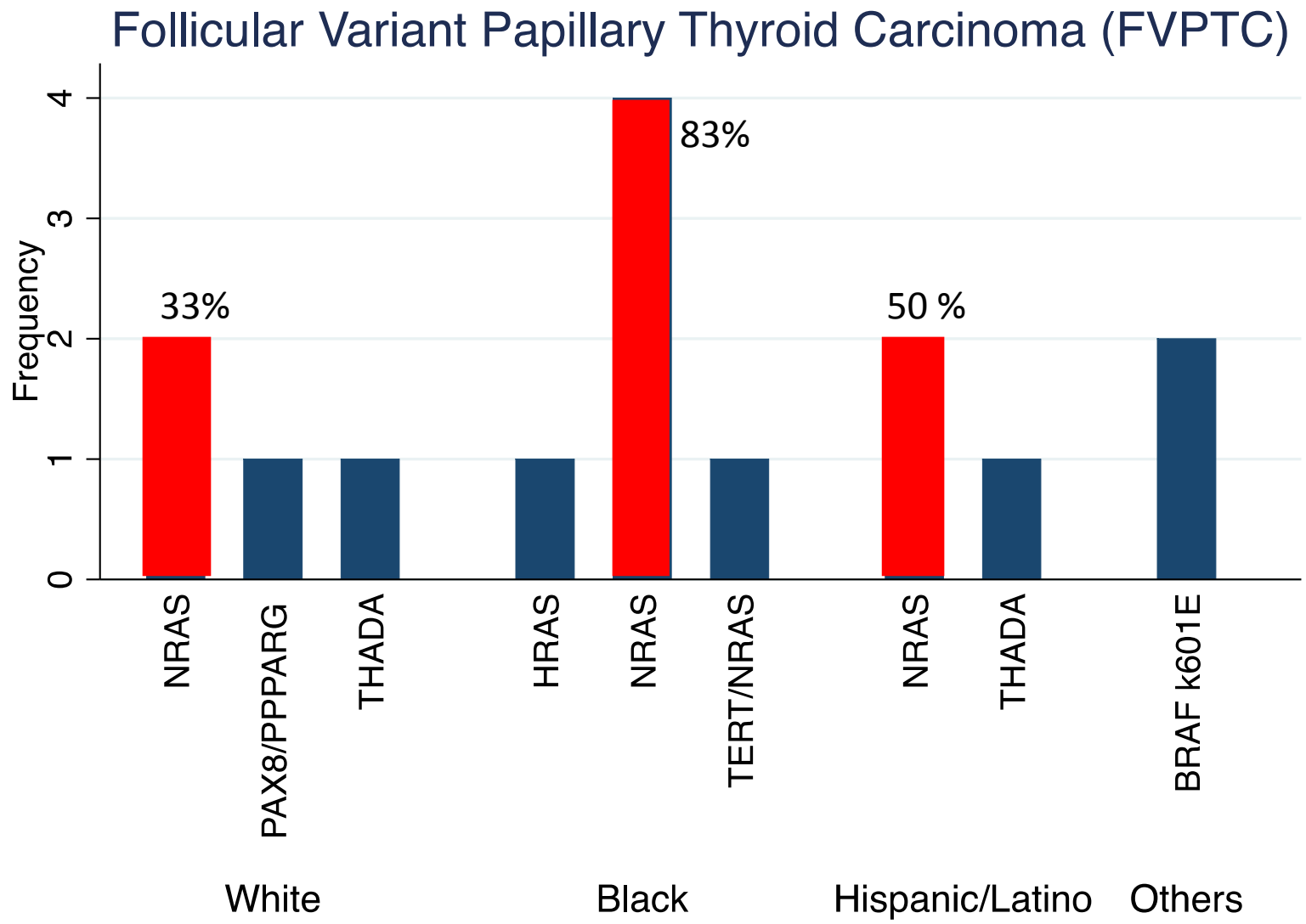
Table 2: Distribution of histopathological subtype of thyroid neoplasm by race/ethnicity subgroup

	Race/ethnicity				
Histological diagnosis of neoplastic nodules	Non-Hispanic white N=31	Non-Hispanic black N=14	Hispanic/Latino N=22	Asian N=7	Others N=7
FA	2	2	5	0	0
FTC	1	1	0	0	0
HA	5	2	0	0	0
MTC	2	2	0	0	0
NIFTP	0	0	2	4	1
PTC	13	1	10	3	3
FVPTC	6	6	4	0	3
PTC-M	1	0	0	0	0
PDC	1	0	1	0	0

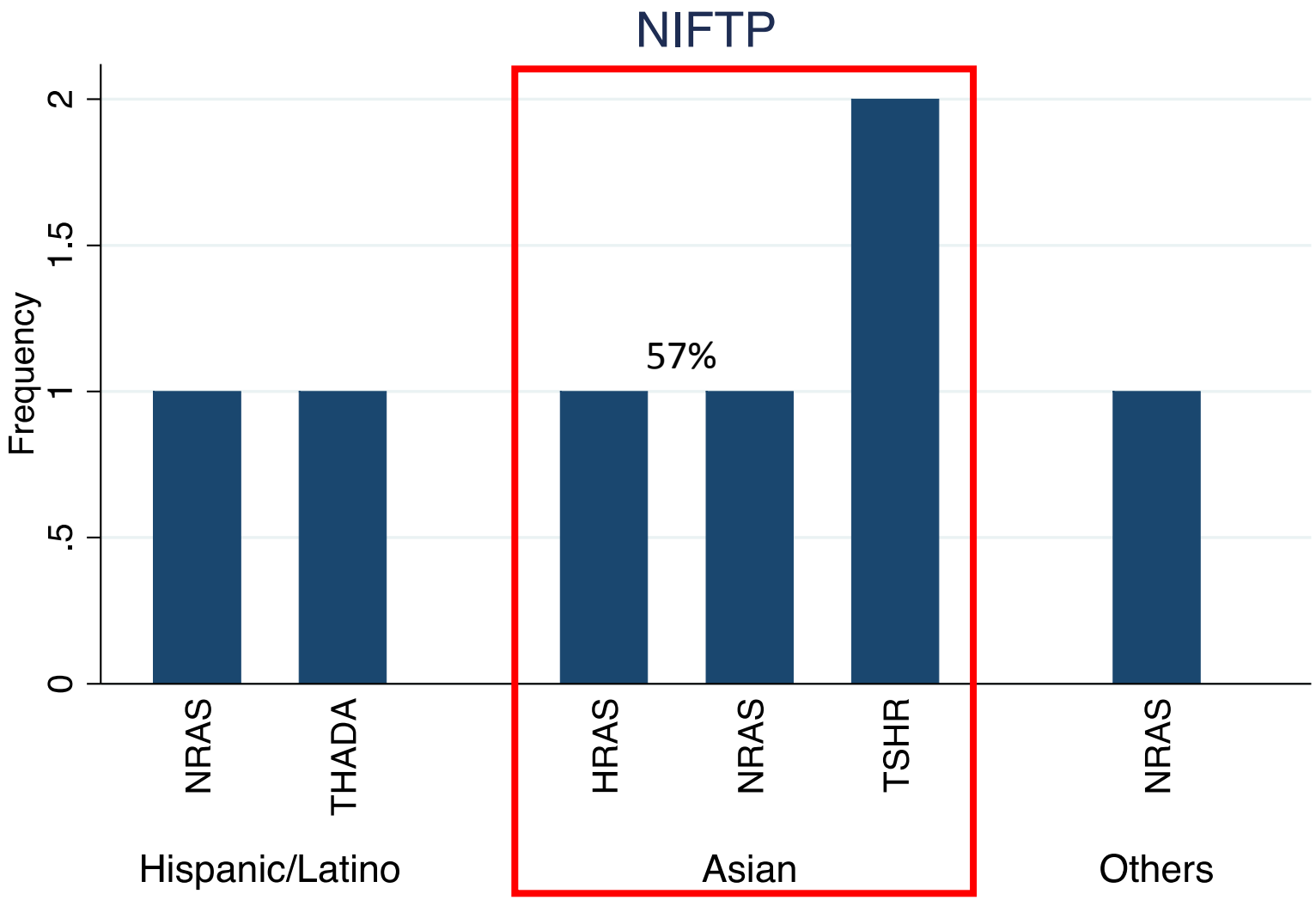
Abbreviations: Follicular Variant Papillary Thyroid Carcinoma FVPTC); Non-invasive Follicular Thyroid Neoplasm with Papillary-like Nuclear Features (NIFTP); Classic Papillary Thyroid Carcinoma (PTC); Papillary Thyroid Microcarcinoma (PTC-M), Follicular Thyroid Carcinoma (FTC); Medullary Thyroid Carcinoma (MTC); Poorly Differentiated Carcinoma (PDC); Follicular Adenoma (FA); Hürthle Cell Adenoma (HA)



NGS was Negative in : Hispanics =3, Asian 1



NGS was Negative in: white =2, Hispanic= 1, other =1



NIFTP: Non-invasive Follicular Thyroid Neoplasm with Papillary-like Nuclear Features

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428 Impact of Racial and Ethnic Differences on the Accurate Classifiction of Thyroid Nodules Using ThyroSeq NextGeneration Sequencing

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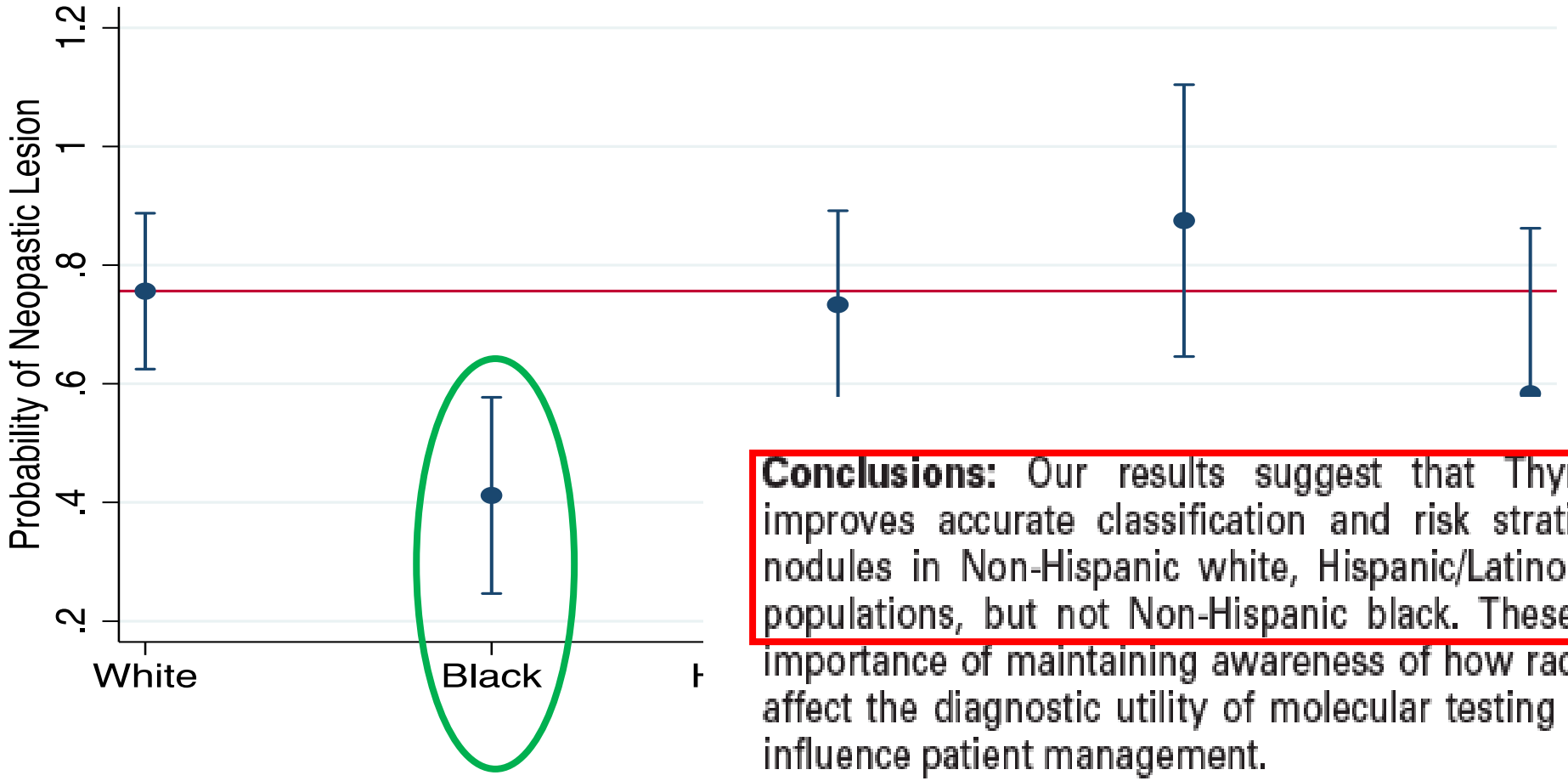
Background: Molecular testing for high risk mutations using Next Generation Sequencing (NGS) (ThyroSeq V2 panel) has been shown to improve classification accuracy of thyroid nodules as neoplastic or non- neoplastic lesions. However, the effects of racial/ethnic disparity on the accurate classification of these nodules is under-studied. In our study, we examined whether racial disparity influences the accuracy of ThyroSeq V2 NGS testing in predicting neoplastic nodules.

	Nodule with Positive ThyroSeq V2		Nodule with Negative ThyroSeq V2			
Race/ethnicity	Neoplastic lesion (n.)	Non-neoplastic lesion (n.)	Neoplastic lesion (n.)	Non-neoplastic lesion (n.)	Odds Ratio[1]	P value
Non-Hispanic white	24	5	7	5	(Reference)	
Non-Hispanic black	11	5	3	15	0.3	0.02
Hispanic/Latino	15	3	7	5	1.1	0.88
Asian	6	0	1	1	2.3	0.49
Unknown/Others	6	3	1	2	0.4	0.26

After adjustment for age, sex, the prevalence of neoplastic lesion in positive ThyroSeq test nodule significantly lower for Non-Hispanic black individuals compared to Non-Hispanic white (Odds ratio, 0.3 [95%CI,0.09-0.8]; P=0.02).



Conclusions: Our results suggest that ThyroSeq significantly improves accurate classification and risk stratification of thyroid nodules in Non-Hispanic white, Hispanic/Latino and Asian patient populations, but not Non-Hispanic black. These results stress the importance of maintaining awareness of how racial differences may affect the diagnostic utility of molecular testing platforms and thus influence patient management.

The adjusted predicted probability of the neoplastic lesion in ThyroSeq positive nodule was significantly lower for Non-Hispanic black compare to other race/ethnic subgroups

Conclusion:

- We found racial/ethnic disparities in the genomic alterations in the subtypes of neoplastic thyroid lesion including prevalence of BRAF and RAS mutations, as well as other oncogenic drivers detected by ThyroSeq test.
- These results stress the importance of maintaining awareness of how racial differences may affect the diagnostic utility of molecular testing platforms and thus influence patient management.

Thank you

Questions?

References:

- Tang, Jianing, et al. "Racial disparities of differentiated thyroid carcinoma: clinical behavior, treatments, and long-term outcomes." *World journal of surgical oncology* 16.1 (2018): 45.
- Laklouk, Israa, et al. "Impact of Racial and Ethnic Differences on the Accurate Classification of Thyroid Nodules Using ThyroSeq Next Generation Sequencing." *MODERN PATHOLOGY*. Vol. 31. 75 VARICK ST, 9TH FLR, NEW YORK, NY 10013-1917 USA: NATURE PUBLISHING GROUP, 2018. http://www.nature.com/articles/labinvest20185.pdf?WT.ec_id=LABINVEST-201803&spMailingID=56232903&spUserID=ODkwMTM2NjMzMQS2&spJobID=1363190854&spReportId=MTM2MzE5MDg1NAS2